

Discovery of Deleterious Genetic Variants in Farmed Animals

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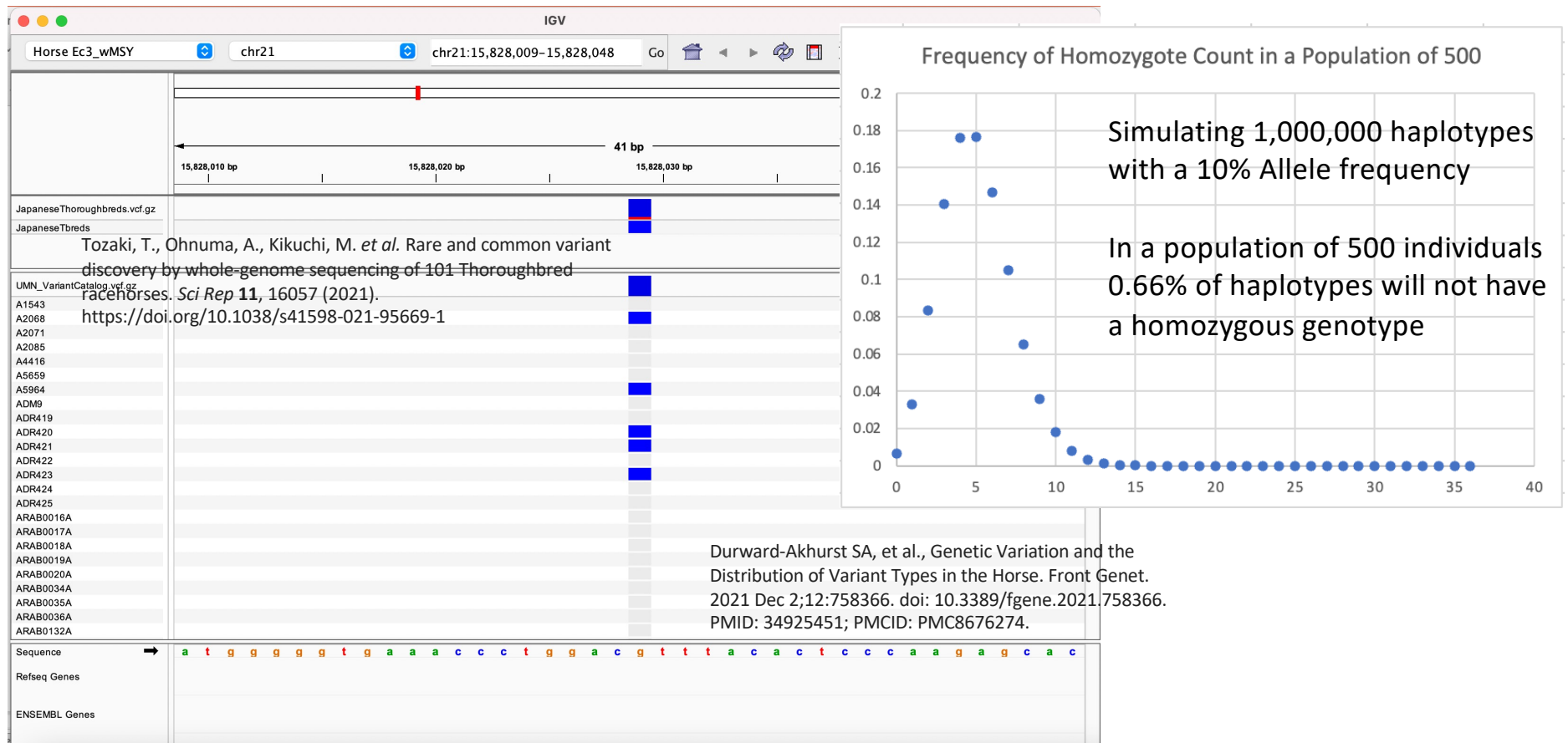


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- Brenda M. Murdoch, Associate Professor, University of Idaho
- David Steffen, Professor, University of Nebraska-Lincoln
- Elaine Norton, Assistant Professor, University of Arizona
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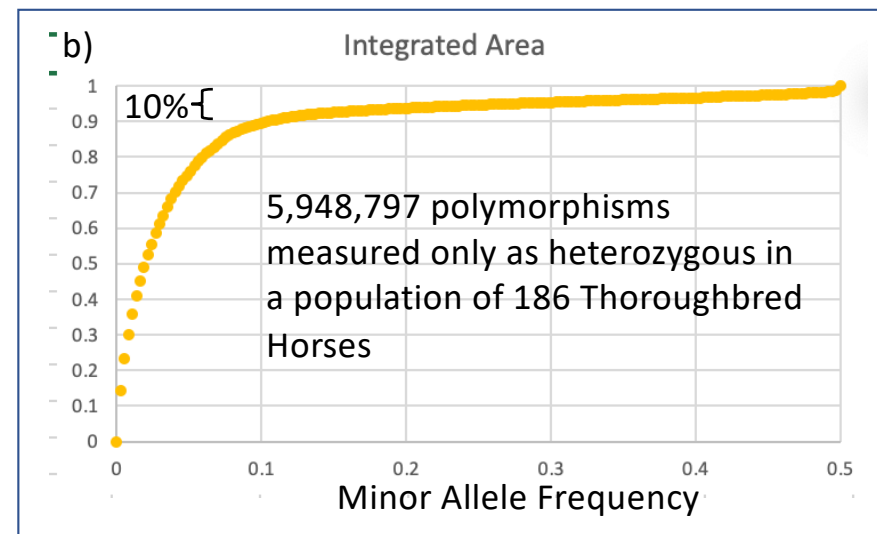
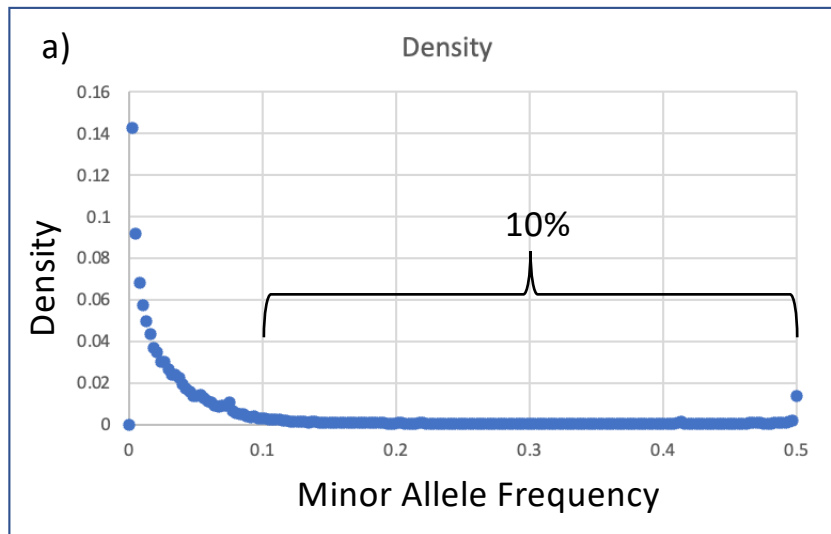
Contributing Students

- Lauren C. Johnson
- Xiomara Arias
- Judith Nikly
- Kailey Ratcliff
- Lindsay Whittaker

Search for Putative Lethal Alleles: An attractive search when you have population level data.



Search for Putative Lethal Alleles: An attractive search when you have population level data.



Assembly Artifacts: Collapsed Duplications

Physical reality:

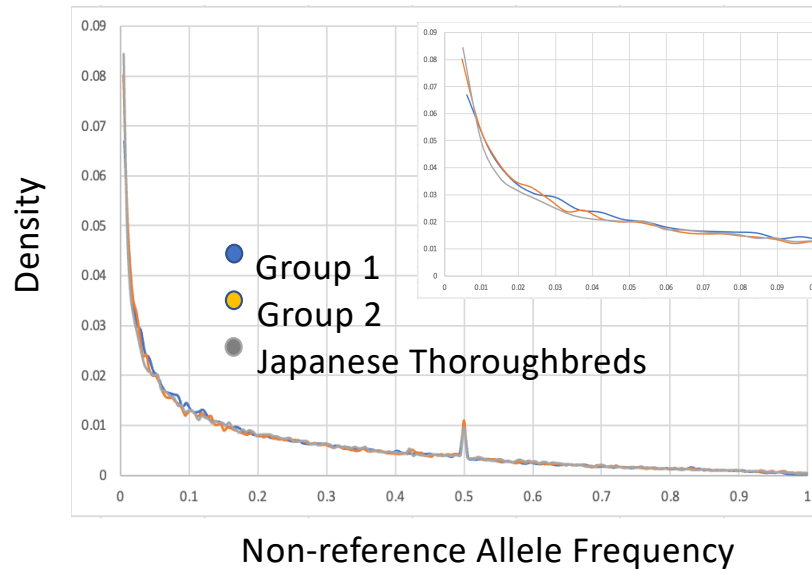
Gene 1

Duplication of Gene 1

Duplication of Gene 1

How this is manifest in an assembly:

Gene 1



Sequencing of Idiopathic Abortions

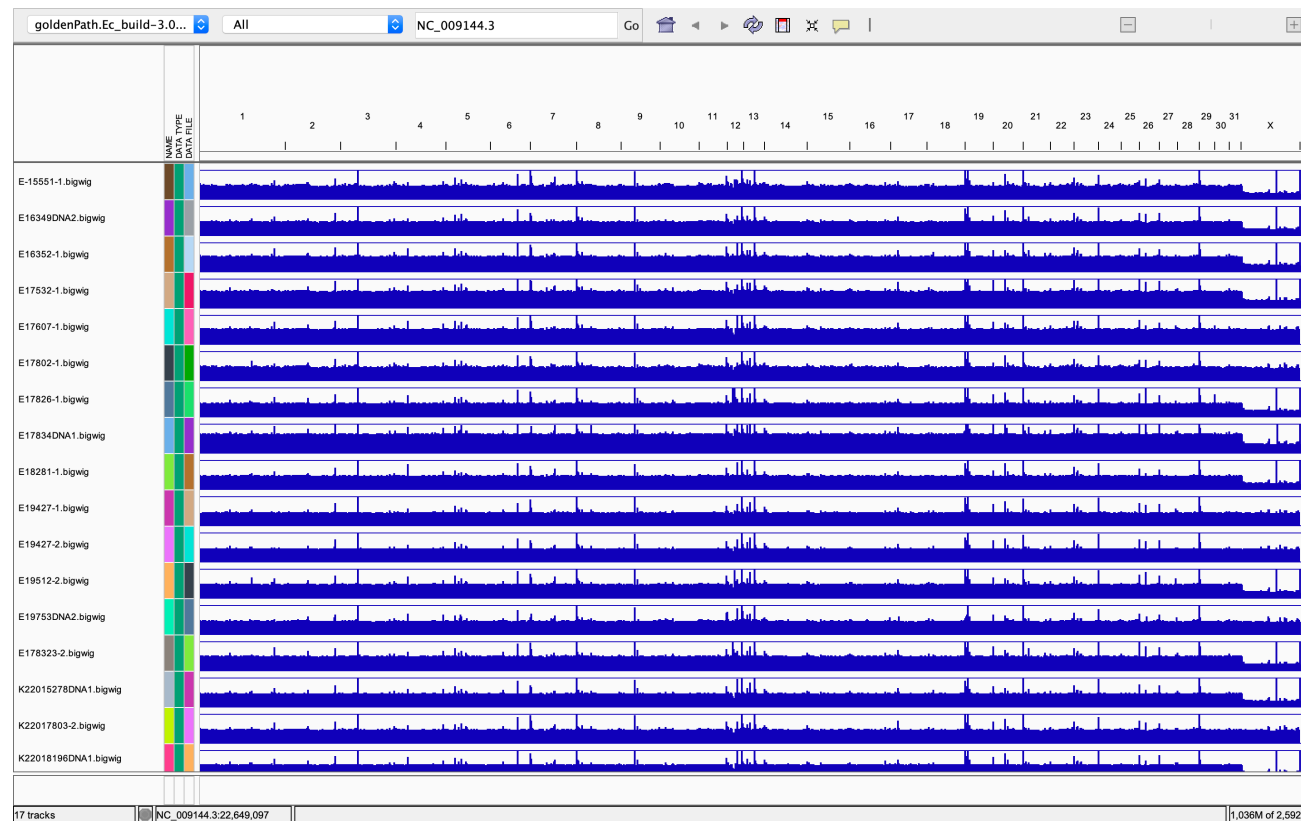
Idiopathic abortion? The animal aborts with no diagnosable etiology for the abortion

Some of these could have genotypes inconsistent with surviving to birth

All samples are later term

What have we developed: You sequence it, we'll do the integrative analysis

Analysis for Aneuploidies



Inbreeding Analysis

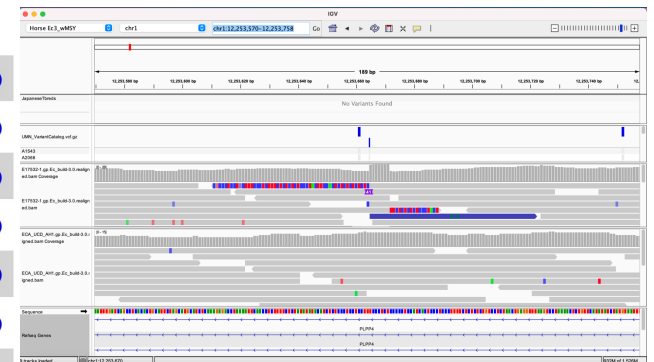
Animal	F
E-15551-1	0.318998
E16349DNA2	0.313206
E16352-1	0.328471
E17532-1	0.332093
E17607-1	0.34469
E17802-1	0.339507
E17826-1	0.292496
E178323-2	0.22322
E17834DNA1	0.30477
E18281-1	0.325326
E19427-1	0.315866
E19427-2	0.316225
E19512-2	0.306187
E19753DNA2	0.312752
K22015278D	
NA1	0.306462
K22017803-2	0.337567
K22018196D	
NA1	0.314953
Tbreds born after 2000	0.321

Outcomes:

https://equinegenomics.uky.edu/data_warehouse/Equus_caballus/Idiopathic_abortions/IdiopathicAbortionSamples.html

All data are mapped to the UCSC Golden Path EquCab3(+MSY).

Idiopathic Abortion Horse Sample	WGS mapped dataset	index	VCF file	index	g.VCF file	index	Filtered VCF file	index
E-15551-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E16349DNA2	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E16352-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E17532-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E17607-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E17802-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E17826-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E178323-2	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E17834DNA1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E18281-1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E19427-2	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E19512-2	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
E19753DNA2	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)
K22015278DNA1	WGS	(index)	VCF	(index)	g.VCF	(index)	Filtered VCF*	(index)



Compelling results of population level data

5 out of 16 Idiopathic abortions homozygous for haplotype with 16% MAF. In a healthy Thoroughbred Population, 3 homozygotes out of 331 animals were measured when 8.7 were expected. This rare haplotype, is, however, fixed in Belgians, and Clydesdales. This locus has been associated with divergent fetal growth in cattle.

JOURNAL ARTICLE

Dissection of Genetic Factors Modulating Fetal Growth in Cattle Indicates a Substantial Role of the Non-SMC Condensin I Complex, Subunit G (NCAPG) Gene ^{FREE}

Annett Eberlein, Akiko Takasuga, Kouji Setoguchi, Ralf Pfuhl, Krzysztof Flisikowski, Ruedi Fries, Norman Klopp, Rainer Fürbass, Rosemarie Weikard, Christa Kühn ✉

Genetics, Volume 183, Issue 3, 1 November 2009, Pages 951–964,

<https://doi.org/10.1534/genetics.109.106476>

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Other results

Other variants enriched in the Idiopathic Abortion cohort, and not found as homozygotes in larger†* populations:

Locus	Animals with Allele				Allele Frequency in 534 horses*
chr2:65482703	3	E17802-1	E178323-2	E19512-2	0.117
chr4:19365862	3	E17802-1	E17826-1	E178323-2	0.023
chr11:58891156	3	E17607-1	E17826-1	E178323-2	0.068
chr21:15693378	3	E16349DNA2	E17802-1	E19427-1	0.035
chr21:15782369	3	E16349DNA2	E17802-1	E19427-1	0.034
chr21:15828029	3	E16349DNA2	E17802-1	E19427-1	0.036
chr21:16262923	3	E16349DNA2	E17802-1	E19427-1	0.029
chr21:16262925	3	E16349DNA2	E17802-1	E19427-1	0.029
chrX:108317357	3	E17532-1	E17826-1	E178323-2	0.063

† Population of 186 Thoroughbreds collected to assess genetic diversity in North American Thoroughbreds, JL Petersen, TS Kalbfleisch, and E Bailey, In process.

* Durward-Akhurst SA, Schaefer RJ, Grantham B, Carey WK, Mickelson JR, McCue ME. Genetic Variation and the Distribution of Variant Types in the Horse. *Front Genet.* 2021 Dec 2;12:758366. doi: 10.3389/fgene.2021.758366. PMID: 34925451; PMCID: PMC8676274.